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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/202,217	09/21/1999	Jean-Luc Dubois	146.1307	2613

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EXAMINER	
GHALI, ISIS A D	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 03/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/202,217	DUBOIS, JEAN-LUC	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25 and 31* is/are pending in the application.

4a) Of the above claim(s) *26-30 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *01/04/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicant's amendment to the claims and specification, IDS, and terminal disclaimer, all filed 01/04/2006.

Claims 26-30 and 32 have been canceled.

Claims 1-25, and 31 are pending and included in the prosecution.

Terminal Disclaimer

1. The terminal disclaimer filed on 01/04/2006 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US application 09/194,996 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The following claims objections are necessitated by applicant's amendment:

Claim Objections

2. Claims 20-23 as amended are objected to as being in improper form because claims 20-23 depends on claim 19, and claims 19 is a multiple dependent claim as it depends on claims 16 and 1-11, and claims 20-23 depend on claim 19, therefore, claim

19 carries out the limitations of claim 16, claim 12 from which claim 16 depends, and claims 1-11. There in no need for applicant to recite that claim 20 is dependent on claim 3, claim 21 is dependent on claim 4, claim 22 is dependent on claim 6, or claim 23 is dependent on claim 7.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Applicant's arguments filed 01/04/2006 with respect to the rejection of claims 1-15 and 31 under 35 U.S.C. 103(a) as being unpatentable over US 4,273,771 ('771) in view of US 5,064,654 ('654) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. The examiner agree that US '654 teaches broad list of active ingredients among which progesterone is cited and among a long list of adhesives, silicone is cited, and it is not obvious to prepare the compositions of the present invention including Trimegestone and silicone matrix by combining US '654 and US '771.

The following rejections are maintained:

5. Claims 1-19 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,904,931 ('931) in view of US 4,273,771 ('771).

US '931 teaches a transdermal therapeutic system for administering a mixture of steroid sex hormones (abstract; col.4, lines 2-4). The system comprises two active ingredients containing matrix layers arranged side by side wherein one matrix is loaded with progesterone and the other is loaded with estrogen (col.6, lines 1-3, 28-32; col.8, example 4). Examples of estrogen include ethinyl estradiol (col.1, lines 27-35; col.12, line 31). The two matrices are separated by space and care must be taken for sufficient spacing of the areas to prevent a diffusion of active ingredient in the respective other area (col.6, lines 36-39). Each matrix is covered by a separate cover layer and the system as a whole is covered by a removable protective layer (Figure 2, col.6, lines 50-57). The system is provided by skin contact adhesive layer (col.4, lines 34-35). The matrix is silicone adhesive or acrylate adhesive (col.5, lines 15-19; col.7, lines 40-43; col.8, example 4). The reference further disclosed that gestagen is used with silicone adhesive and estrogen is used with polyacrylate adhesive (col.7, example 1; col.8, lines 35-38).

US '931 does not teach the progesterone to be Trimegestone.

US '771 teaches Trimegestone to be delivered topically to the skin (col.4, lines 34-36, 58; col.5, lines 46-49). Trimegestone is useful to treat dysmenorrheal, sterility, ovarian dystrophia, and uterine tumors and useful as contraceptive (col.4, lines 45-49).

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal therapeutic system comprising two

adhesive matrices, one loaded with progesterone and the other loaded with estrogen as disclosed by US '931, and replace estrogen by Trimegestone disclosed by US '771, motivated by the teaching of US '771 that Trimegestone is useful to treat dysmenorrheal, sterility, ovarian dystrophia, and uterine tumors and useful as contraceptive, with reasonable expectation of having transdermal therapeutic system that deliver Trimegestone and estrogen from two separate matrices to the patient in need of such treatment.

Response to Arguments

6. Applicant's arguments filed 01/04/2006 have been fully considered but they are not persuasive. Applicant traverses this rejection by arguing that the US '931 teaches transdermal device containing progesterone and possible estradiol derivative in a matrix, but does not suggest a device similar to the present one. US '771 teaches Trimegestone may be topically applied but only in very general manner and does not suggest administration in the form of a patch.

In response to applicant's arguments, applicant attention is directed to the scope of the present claims which are drawn to transdermal patch comprising a silicone matrix to deliver a progesterone derivative and further comprises an acrylic matrix to deliver estrogen or derivatives thereof. US '931 in example 1 teaches progesterone delivered transdermally in silicone matrix, and example 4 teaches estrogen delivered in acrylic matrix. The device disclosed by US '931 is very similar in structure to the present device as evident from figure 2 of the reference which is similar to figure 4 of the present invention. As applicant admits, the device disclosed by US '931 delivers both

progesterone and estrogen. Indeed, US '931 teaches the delivery of progesterone in silicone matrix and estrogen in acrylic matrix, both in a device having the same structure as instantly claimed. The only difference between US '931 and the present invention is that the reference does not teach the species of progesterone (Trimegestone). US '771 is relied upon for the solely teaching of Trimegestone suitable for transdermal delivery. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to replace the progesterone in the transdermal device disclosed by US '931 by Trimegestone disclosed by US '771. Motivation would arise from the teaching of US '771 that Trimegestone is useful for treating the same syndromes applicant desired to treat including dysmenorrheal, sterility, ovarian dystrophia, and uterine tumors and useful as contraceptive, with reasonable expectation of having transdermal therapeutic system that deliver Trimegestone and estrogen from two separate matrices to the patient in need of such treatment. A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969).

In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the claims would have been *prima facie* obvious within the meaning of 35 U.S.C. 103 (a).

7. Claims 1-19 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,858,394 ('394) in view of US '771.

US '394 teaches a transdermal therapeutic system for administering a mixture of steroid sex hormones (abstract; col.1, lines 41-44). The system comprises two active ingredients containing matrix layers arranged side by side wherein one matrix is loaded with gestodene and the other is loaded with estrogen (col.5, lines 11-16, 38-45; col.8, example 4). Examples of estrogen include ethinyl estradiol (col.2, lines 10-12; col.10, line 44). The two matrices are separated by space and care must be taken for sufficient spacing of the areas to prevent a diffusion of active ingredient in the respective other area (col.5, lines 20-23). Each matrix is covered by a separate cover layer and the system as a whole is covered by a removable protective layer (Figure 2, col.5, lines 38-45). The system is provided by skin contact adhesive layer (col.4, lines 13-14). The matrix is silicone adhesive or acrylate adhesive (col.4, lines 16-19; col.6, lines 66-67; col.8, example 4). The reference further disclosed that gestagen is used with silicone adhesive and estrogen is used with polyacrylate adhesive (col.6, example 1; col.8, lines 7-10). The reference disclosed that the individual reservoirs are provided with differing permeable polymers to adapt the diffusion flow of the individual active ingredients to the respective need (col.5, lines 23-27).

US '394 does not teach the progesterone to be Trimegestone.

US '771 teaches Trimegestone to be delivered topically to the skin (col.4, lines 34-36, 58; col.5, lines 46-49). Trimegestone is useful to treat dysmenorrheal, sterility, ovarian dystrophia, and uterine tumors and useful as contraceptive (col.4, lines 45-49).

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal therapeutic system comprising two

adhesive matrices, one loaded with progesterone and the other loaded with estrogen as disclosed by US '394, and replace estrogen by Trimegestone disclosed by US '771, motivated by the teaching of US '771 that Trimegestone is useful to treat dysmenorrheal, sterility, ovarian dystrophia, and uterine tumors and useful as contraceptive, with reasonable expectation of having transdermal therapeutic system that deliver Trimegestone and estrogen from two separate matrices to the patient in need of such treatment.

Response to Arguments

8. Applicant repeats the same arguments for this rejection as for US '931 in view of US '771. Therefore, the same response is repeated.

9. Claims 1-19 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,296,230 ('230) in view of US '771.

US '230 teaches a transdermal fertility control system comprising multi-region transdermal delivery dosage unit and method of its making (abstract). The dosage unit delivers different steroid hormones from different regions within a single dosage unit (col.16, lines 63-68). The different regions have different shapes (col.18, lines 66-68). The dosage unit contains the hormones in a matrix made of silicon adhesive polymer (col.3, lines 55-62). The reference discloses that factors can be changed to control the amount or ratio of hormones delivered from the system, and among these factors are the area and area ratio of each region, and changing the type of polymer adhesive which forms each region (col.17, lines 16-23). Hormones to be delivered by the

disclosed system is combination of 17beta-estradiol and progesterone, such as megestone (col.4, lines 6-7; col.12, lines 29-30).

US '230 does not teach the progesterone to be Trimegestone.

US '771 teaches Trimegestone to be delivered topically to the skin (col.4, lines 34-36, 58; col.5, lines 46-49). Trimegestone is useful to treat dysmenorrheal, sterility, ovarian dystrophia, and uterine tumors and useful as contraceptive (col.4, lines 45-49).

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal therapeutic system comprising two adhesive matrices, one loaded with progesterone and the other loaded with estrogen as disclosed by US '230, and replace estrogen by Trimegestone disclosed by US '771, motivated by the teaching of US '771 that Trimegestone is useful to treat dysmenorrheal, sterility, ovarian dystrophia, and uterine tumors and useful as contraceptive, with reasonable expectation of having transdermal therapeutic system that deliver Trimegestone and estrogen from two separate matrices to the patient in need of such treatment.

Response to Arguments

10. Applicant repeats the same arguments for this rejection as for US '931 in view of US '771. Therefore, the same response is repeated.

11. Claims 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of US '931, US '394 and US '230 in view of US '771 as applied to claims 1-19 and 31 above, and further in view of WO93/10772 ('772).

The teachings of US '931, US '394 and US '230 each in combination with US '771 are discussed above. However, the combination of the references do not teach the species of the acrylate used with the estradiol to be 2-ethylhexyl acrylate and vinyl acetate copolymer.

WO '772 teaches transdermal delivery system to deliver 17beta-estradiol to the skin said system comprises the drug in 2-ethylhexyl acrylate and vinyl acetate copolymer matrix (abstract). The system is well-tolerated, stable, effective, prevents crystallization of the drug and ensures adequate extended level of active ingredient in the blood and has good tack and adhesive properties (pages 5 and 6).

Thus, it would have been obvious to one having ordinary skill in the art a the time of the invention to provide a transdermal drug delivery device to deliver Trimegestone and 17beta-estradiol as disclosed by the combination of the above references, and select 2-ethylhexyl acrylate and vinyl acetate copolymer matrix to deliver the estradiol, motivated by the teaching of WO '772 that the 2-ethylhexyl acrylate and vinyl acetate copolymer matrix is well tolerated, stable, effective, prevents crystallization of estradiol and ensures adequate extended level of the hormone in the blood and has good tack and adhesive properties, with reasonable expectation of the delivered device to provide the combination of hormones from two different matrices with success.

Response to Arguments

12. Applicant has failed to traverse this rejection. The rejection is therefore repeated for reasons of record.

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US '654 teaches transdermal device to provide enhanced drugs flux and meanwhile is well tolerated (abstract; col.2, lines 15-23). The device comprises progesterone in a silicone matrix, and further comprises silicone fluid as a plasticizer (col.4, lines 48, 66-68; col.5, lines 25-31; col.10, example 1). The device comprises backing layer, a membrane layer and skin contact adhesive layer of silicone (col.3, lines 29-30; col.7, lines 37-43; example 1).

Conclusion

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Isis Ghali
Examiner
Art Unit 1615

IG

Isis Ghali